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(54) QUINOLINE DERIVATIVES AND QUINAZOLINE DERIVATIVES INHIBITING AUTOPHOSPHORYLATION OF GROWTH FACTOR RECEPTOR ORIGINATING IN PLATELET AND PHARMACEUTICAL COMPOSITIONS CONTAINING THE SAME

(57) The present invention relates to novel quinoline derivatives and quinazoline derivatives represented by the following formula (I):

EP 0 860 433 A1

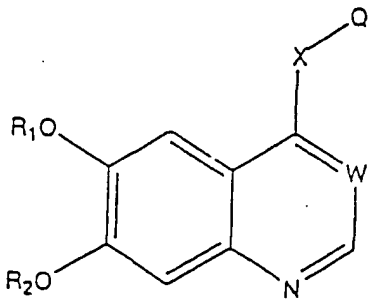
The results shown above revealed that the compound number 43 suppressed the incidence of collagen-induced arthritis.

Possible Industrial Use

Since the compounds of the present invention have inhibitory activity on abnormal cell growth, more specifically PDGF receptor autophosphorylation inhibitory activity, they are useful for treating numerous diseases such as leukemia, cancers, psoriasis, glomerulonephritis, organofibrosis, atherosclerosis, restenosis after percutaneous coronary angioplasty or bypass surgery and articular rheumatism. Therefore, the compounds can benefit greatly in treating humans and other animals which need these treatments.

Claims

1. Quinoline derivatives and quinazoline derivatives represented by the following formula (I):

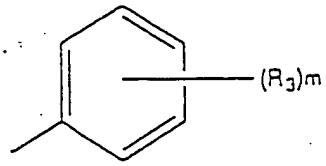


(I)

{wherein R_1 and R_2 are each independently H, C_1-C_5-alkyl, or R_1 and R_2 together form C_1-C_3-alkylene, and W is CH or N,

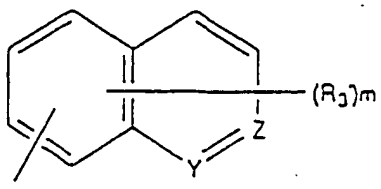
(1) when W is CH,

(a) X is O or S, and Q is a phenyl group represented by formula (II):



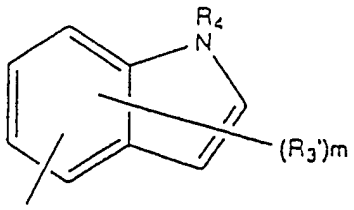
(II)

[wherein m is 1, 2 or 3, R_3 is each independently CN, OH, halogen, C_1-C_5-alkyl, C_1-C_4-alkoxy or C_2-C_4-acyl],
a group represented by formula (III):



(III)

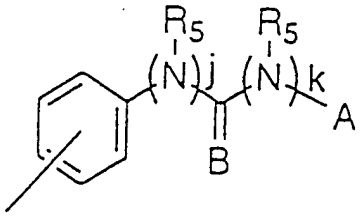
[wherein m is as defined as described above, R_3' is each independently OH, C_1-C_5-alkyl, C_1-C_4-alkoxy, and Y and Z are both or each independently N or CH],
or a group represented by formula (IV):



(IV)

[wherein m and R_3' are as defined as described above, and R_4 is H, C_1-C_5-alkyl or C_2-C_4-acyl], and

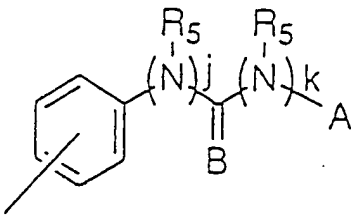
(b) X is O, S or CH_2, and Q is a group represented by formula (V):



(V)

[wherein j and k are each independently 0 or 1, R_5 is each independently H or C_1-C_4-alkyl, A is C_1-C_8-alkyl, C_1-C_5-alkenyl, cyclic (C_3-C_{10}) alkyl, C_1-C_4-alkoxycarbonyl, phenyl, naphthyl, furyl, thienyl, benzoyl, substituted benzoyl, C_2-C_4-acyl, or 5- or 6-membered monocyclic or 9- or 10-membered bicyclic heteroaryl group having 1 or 2 nitrogen atoms and optionally having another hetero atom selected from the group consisting of nitrogen, oxygen and sulfur atoms, these alkyl group, aryl group and heteroaryl group represented by A may have 1 to 5 substituents selected from the group consisting of CN, NO_2, OH, NH_2, halogen, C_1-C_5-alkyl, cyclic (C_3-C_{10}) alkyl, C_1-C_4-alkoxy, C_1-C_4-alkoxycarbonyl, C_1-C_5-acyl, C_1-C_5-acyloxy, C_1-C_3-alkylenedioxy, C_1-C_4-alkylamino, di-(C_1-C_4-alkyl)amino, CO_2H, $CONH_2$, N-(C_1-C_4-alkyl)amido, N,N-di-(C_1-C_4-alkyl)amido, C_2-C_4-alkylamido, trifluoromethyl, C_1-C_4-alkylthio, phenyl, substituted phenyl, phenoxy, substituted phenoxy, phenylthio, substituted phenylthio, phenyl(C_1-C_4-alkyl), substituted phenyl(C_1-C_4-alkyl), pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, pyrrolidinyl, piperidinyl, piperazinyl, homopyperazinyl, morpholinyl, quinolyl, quinazolinyl, benzoyl, substituted benzoyl and C_2-C_4-acyl, and B is O, S, NH, NCN, NR_6 or NOR_6 (wherein R_6 is C_1-C_5-alkyl)],

(2) when W is N, X is O, S or CH_2, and Q is represented by formula (V):



(V)

[wherein j, k, R_5, A and B are defined as described above]} and pharmaceutically acceptable salts thereof.

2. Quinoline derivatives and pharmaceutically acceptable salts thereof according to Claim 1, characterized in that in formula (I), W is CH, X is O or S, and Q is formula (II), formula (III) or formula (IV).

3. Quinoline derivatives and pharmaceutically acceptable salts thereof according to Claim 1, characterized in that in formula (I), W is CH, X is O, and Q is formula (II), formula (III) or formula (IV).

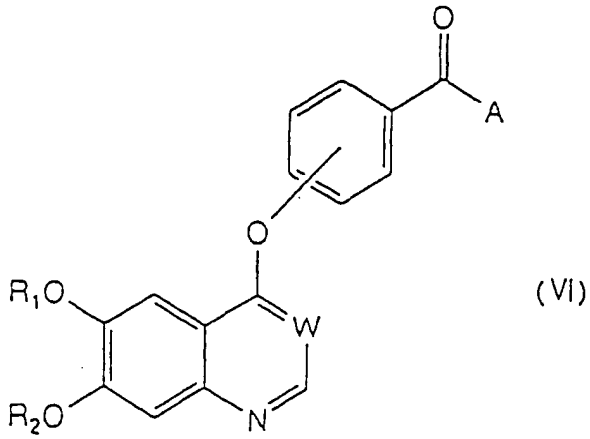
4. Quinoline derivatives and quinazoline derivatives and pharmaceutically acceptable salts thereof according to Claim 1, characterized in that in formula (I), X is O, S or CH_2, and Q is formula (V).

5. Quinoline derivatives and quinazoline derivatives and pharmaceutically acceptable salts thereof according to Claim 1, characterized in that in formula (I), R_1 and R_2 are each independently C_1-C_5-alkyl and Q is formula (V) [in formula (V), j and k are 0, B is O, S, NOR_6 (wherein R_6 is C_1-C_5-alkyl)].

6. Quinoline derivatives and quinazoline derivatives and pharmaceutically acceptable salts thereof according to Claim 1, characterized in that in formula (I), R_1 and R_2 are each independently C_1-C_5-alkyl and Q is formula (V) [in formula (V), j is 0 and k is 1, or j is 1 and k is 0, R_5 is hydrogen or methyl, B is O, S, NH, NCN, NR_6 or NOR_6 (wherein R_6 is C_1-C_5-alkyl)].

7. Quinoline derivatives and quinazoline derivatives and pharmaceutically acceptable salts thereof according to Claim 1, characterized in that in formula (I), R_1 and R_2 are each independently C_1-C_5-alkyl and Q is formula (V) [in formula (V), both j and k are 1, R_5 is each independently hydrogen or methyl, B is O, S, NH, NCN, NR_6 or NOR_6 (wherein R_6 is C_1-C_5- alkyl)].

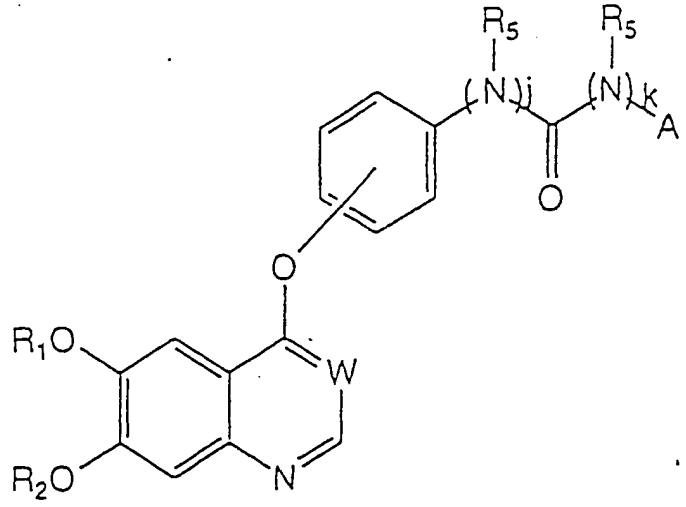
8. Quinoline derivatives and quinazoline derivatives of formula (VI)



(VI)

[wherein W is CH or N, R_1 and R_2 are each independently C_1-C_5-alkyl, A is methyl, ethyl, propyl, isopropyl, butyl, isobutyl, s-butyl, t-butyl, pentyl, isopentyl, cyclopentyl, cyclohexyl, cycloheptyl, phenyl, naphthyl, furyl, thienyl, pyridyl or pyrimidinyl, and these alkyl group, aryl group or heteroaryl group represented by A may have 1-5 substituents selected from the group consisting of fluoro, chloro, bromo, iodo, cyano, hydroxy, nitro, amino, methylamino, dimethylamino, diethylamino, dipropylamino, dibutylamino, trifluoromethyl, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, s-butyl, t-butyl, methoxy, ethoxy, propoxy, isopropoxy, morpholino, pyrrolidino, piperidino and butoxy] and pharmaceutically acceptable salts thereof.

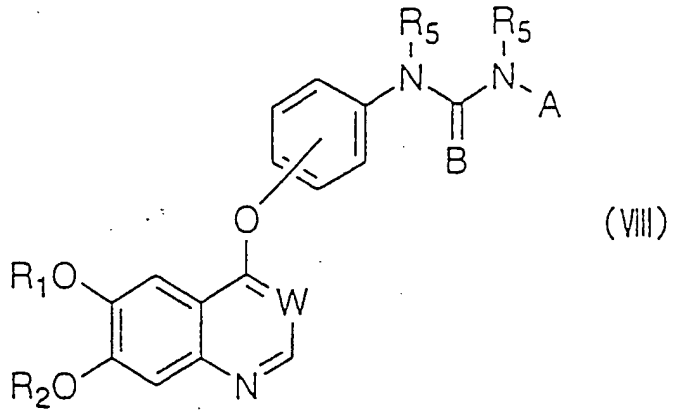
9. Quinoline derivatives and quinazoline derivatives formula (VII)



(VII)

[wherein W is CH or N, j is 0 and k is 1 or j is 1 and k is 0, R_1 and R_2 are each independently C_1-C_5-alkyl, R_5 is hydrogen or methyl, A is methyl, ethyl, propyl, isopropyl, butyl, isobutyl, s-butyl, t-butyl, pentyl, isopentyl, cyclopentyl, cyclohexyl, cycloheptyl, phenyl, naphthyl, furyl, thienyl, pyridyl or pyrimidinyl, and these alkyl group, aryl group or heteroaryl group represented by A may have 1-5 substituents selected from the group consisting of fluoro, chloro, bromo, iodo, cyano, hydroxy, nitro, amino, methylamino, dimethylamino, diethylamino, dipropylamino, dibutylamino, trifluoromethyl, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, s-butyl, t-butyl, methoxy, ethoxy, propoxy, isopropoxy and butoxy] and pharmaceutically acceptable salts thereof.

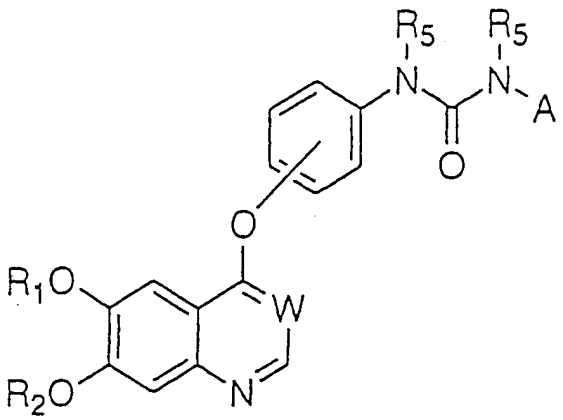
10. Quinoline derivatives and quinazoline derivatives of formula (VIII)



(VIII)

[wherein W is CH or N, R_1 and R_2 are each independently C_1-C_5-alkyl, R_5 is each independently hydrogen or methyl, A is C_1-C_6-alkyl, C_1-C_4-alkenyl, cyclopentyl, cyclohexyl, cycloheptyl, C_1-C_4-alkoxycarbonyl, phenyl, naphthyl, furyl, thienyl, benzoyl, acetyl, pyridyl, pyrimidinyl, pyrrolidinyl, piperidinyl, piperazinyl, homopiperazinyl or morpholino, these alkyl group, aryl group or heteroaryl group represented by A may have 1-5 substituents selected from the group consisting of halogen, cyano, CO_2H, $CONH_2$, hydroxy, nitro, amino, C_1-C_4-alkylamino, di-(C_1-C_4-alkyl)amino, C_1-C_5-acyloxy, C_1-C_5-acyl, C_1-C_4-alkylthio, trifluoromethyl, C_1-C_5-alkyl, C_1-C_4-alkoxyl, C_1-C_4-alkoxycarbonyl, N-(C_1-C_4-alkyl)amido, N,N-di-(C_1-C_4-alkyl)amido, C_2-C_4-alkylamido, ethylenedioxy, phenyl, phenoxy, substituted phenyl, benzoyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, quinolyl and quinazolinyl, and B is O, S, NH, NCN, NR_6 or NOR_6 (in which R_6 is methyl)] and pharmaceutically acceptable salts thereof.

11. Quinoline derivatives and quinazoline derivatives of formula (IX)



(IX)

[wherein W is CH or N, R_1 and R_2 are each independently C_1-C_5-alkyl, R_5 is each independently hydrogen or methyl, A is C_1-C_6-alkyl, C_1-C_4-alkenyl, cyclopentyl, cyclohexyl, cycloheptyl, C_1-C_4-alkoxycarbonyl, phenyl, naphthyl, furyl, thienyl, benzoyl, acetyl, pyridyl, pyrimidinyl, pyrrolidinyl, piperidinyl, piperazinyl, homopiperazinyl or morpholino, and these alkyl group, aryl group or heteroaryl group represented by A may have 1-5 substituents selected from the group consisting of halogen, cyano, CO_2H, $CONH_2$, hydroxy, nitro, amino, C_1-C_4-alkylamino, di-(C_1-C_4-alkyl)amino, C_1-C_5-acyloxy, C_1-C_5-acyl, C_1-C_4-alkylthio, trifluoromethyl, C_1-C_5-alkyl, C_1-C_4-alkoxyl, C_1-C_4-alkoxycarbonyl, N-(C_1-C_4-alkyl)amido, N,N-di-(C_1-C_4-alkyl)amido, C_2-C_4-alkylamido, ethylenedioxy, phenyl, phenoxy, substituted phenyl, benzoyl, pyridyl, pyrazinyl, pyrimidinyl pyridazinyl, quinolyl and quinazolinyl] and pharmaceutically acceptable salts thereof.

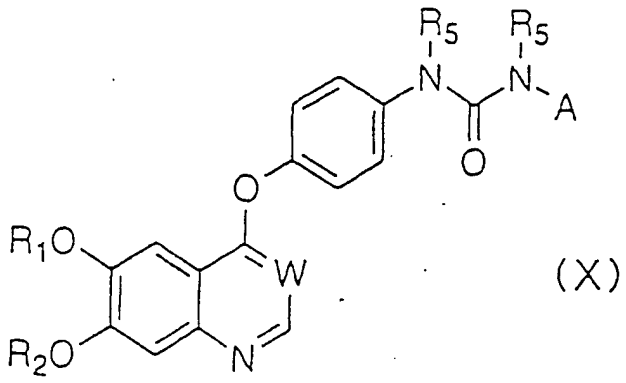
12. Quinoline derivatives and pharmaceutically acceptable salts thereof according to Claim 8, characterized in that in formula (VI), W is CH.

13. Quinoline derivatives and pharmaceutically acceptable salts thereof according to Claim 9, characterized in that in formula (VII), W is CH.

14. Quinoline derivatives and pharmaceutically acceptable salts thereof according to Claim 10, characterized in that in formula (VIII), W is CH.

15. Quinoline derivatives and pharmaceutically acceptable salts thereof according to Claim 11, characterized in that in formula (IX), W is CH.

16. Quinoline derivatives and quinazoline derivatives of formula (X)

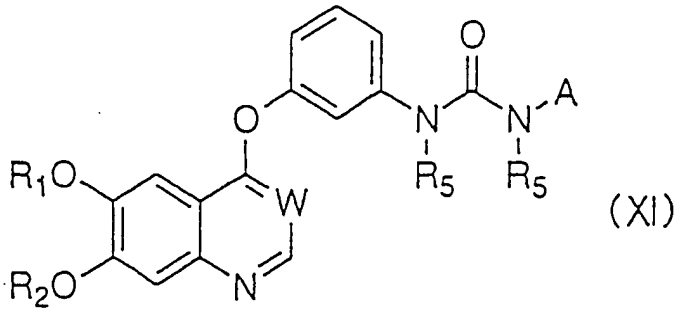


(X)

[wherein W is CH or N, R_1 and R_2 are each independently C_1-C_5-alkyl, R_5 is each independently hydrogen or methyl, A is C_1-C_5-alkyl, cyclopentyl, cyclohexyl, cycloheptyl, allyl, C_1-C_4-alkoxycarbonyl, phenyl, naphthyl or ben-

zoyl, and these alkyl group or aryl group represented by A may have 1-5 substituents selected from the group consisting of OH, CO_2H, fluoro, chloro, bromo, iodo, nitro, amino, di-(C_1-C_4-alkyl)amino, ethylenedioxy, acetoxy, methylthio, C_1-C_4-alkoxycarbonyl, trifluoromethyl, C_1-C_4-alkyl, pyridyl and phenyl]
and pharmaceutically acceptable salts thereof.

17. Quinoline derivatives and quinazoline derivatives of formula (XI)



(XI)

[wherein W is CH or N, R_1 and R_2 are each independently C_1-C_5-alkyl, R_5 is each independently hydrogen or methyl, A is C_1-C_5-alkyl, cyclopentyl, cyclohexyl, cycloheptyl, allyl, C_1-C_4-alkoxycarbonyl, phenyl, naphthyl or benzoyl, and these alkyl group or aryl group represented by A may have 1-5 substituents selected from the group consisting of OH, CO_2H, fluoro, chloro, bromo, iodo, nitro, amino, di-(C_1-C_4-alkyl)amino, ethylenedioxy, acetoxy, methylthio, C_1-C_4-alkoxycarbonyl, trifluoromethyl, C_1-C_4-alkyl, C_1-C_4-alkoxy, pyridyl and phenyl],
and pharmaceutically acceptable salts thereof.

18. Quinoline derivatives and quinazoline derivatives according to Claim 1, characterized in that in formula (I), W is CH, X is O, both R_1 and R_2 are methyl, Q is formula (V) [in formula (V), j and k are each independently 0 or 1, R_5 is hydrogen, A is C_1-C_5-alkyl, cyclopentyl, cyclohexyl, cycloheptyl, allyl, C_1-C_4-alkoxycarbonyl, phenyl, naphthyl or benzoyl, these alkyl group, aryl group or heteroaryl group represented by A may have 1-5 substituents selected from the group consisting of OH, CO_2H, fluoro, chloro, bromo, iodo, nitro, amino, di-(C_1-C_4-alkyl)amino, ethylenedioxy, acetoxy, methylthio, C_1-C_4-alkoxycarbonyl, trifluoromethyl, C_1-C_4-alkyl, C_1-C_4-alkoxy, pyridyl and phenyl, and B is O, S, NH, NCN, NR_6 or NOR_6 (in which R_6 is methyl)]
and pharmaceutically acceptable salts thereof.

19. Compounds according to Claim 16, characterized in that in formula (I), W is CH, both R_1 and R_2 are methyl, and each R_5 is hydrogen, and pharmaceutically acceptable salts thereof.

20. Compounds of formula (I) according to Claim 1 selected from 6,7-dimethoxy-4-(2-methoxyphenoxy)quinoline, 6,7-dimethoxy-4-(3-methoxyphenoxy)quinoline, 6,7-dimethoxy-4-(4-methoxyphenoxy)quinoline, 4-(3-fluorophenoxy)-6,7-dimethoxyquinoline, 4-(3-hydroxyphenoxy)-6,7-dimethoxyquinoline, 4-(4-bromophenoxy)-6,7-dimethoxyquinoline, 4-(3,4-dimethoxyphenoxy)-6,7-dimethoxyquinoline, 6,7-dimethoxy-4-(1-naphthyloxy)quinoline, 6,7-dimethoxy-4-(2-naphthyloxy)quinoline, 6,7-dimethoxy-4-(5-methoxy-1-naphthyloxy)quinoline, 6,7-dimethoxy-4-(6-methoxy-2-naphthyloxy)quinoline, 6,7-dimethoxy-4-(7-methoxy-2-naphthyloxy)quinoline, 6,7-dimethoxy-4-(5-quinolyloxy)quinoline, 6,7-dimethoxy-4-(6-quinolyloxy)quinoline, 4-(4-indolyloxy)-6,7-dimethoxyquinoline, 4-(5-indolyloxy)-6,7-dimethoxyquinoline, 6,7-dimethoxy-4-(3-methoxyphenylthio)quinoline and 6,7-dimethoxy-4-(4-methoxyphenylthio)quinoline,
and pharmaceutically acceptable salts thereof.

21. Compounds of formula (I) according to Claim 1 selected from (4-n-butylphenyl){4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}methanone, (4-t-butylphenyl){4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}methanone, (4-trifluoromethylphenyl){4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}methanone, (4-t-butylphenyl){4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}methanone, (4-t-butylphenyl){4-[(6,7-dimethoxy-4-quinolyl)methyl]phenyl}methanone, N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-cyclohexanecarboxamide, N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-(4-nitrophenyl)carboxamide, N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-(N,N-dimethylaminophenyl)carboxamide, N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-(4-acetylphenyl)carboxamide, N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-(4-n-butylphenyl)carboxamide, N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-(4-butoxy-

phenyl)carboxamide, N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-(4-bromophenyl)carboxamide, N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}cyclopontanecarboxamide, N-(4-n-butylphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(4-t-butylphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(2-trifluoromethylphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(3-trifluoromethylphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(4-trifluoromethylphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(2-methoxyphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(4-methoxyphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(2-fluorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(3-fluorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(4-fluorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(4-acetylphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-n-propylurea, N-n-butyl-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}phenylurea, N-(2-fluorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}urea, N-(2-methoxyphenyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}urea, N-(4-methoxyphenyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}urea, N-n-butyl-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}urea, {4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}[4-morpholinophenyl]methanone, {4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}[4-pyrrolidinophenyl]methanone, {4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}[4-piperidinophenyl]methanone, N-(2,4-dichlorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(3,4-dichlorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(3,5-dichlorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(4-chloro-2-methylphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(3-amino-4-chlorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-pyridylmethyl)urea, N-(3,4-difluorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(2,4,5-trifluorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(3-chlorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea and N-(4-hydroxyphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, and pharmaceutically acceptable salts thereof.

22. A pharmaceutical composition which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and pharmaceutically acceptable salts thereof according to any one of Claims 1-21 having platelet-derived growth factor receptor autophosphorylation inhibitory activity.

23. A pharmaceutical composition for use in treating tumors, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 1-21.

24. A pharmaceutical composition for use in treating psoriasis, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 1-21.

25. A pharmaceutical composition for use in treating atherosclerosis, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 1-21.

26. A pharmaceutical composition for use in treating restenosis after percutaneous coronary angioplasty or bypass surgery, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 1-21.

27. A pharmaceutical composition for use in treating glomerulonephritis, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 1-21.

28. A pharmaceutical composition for use in treating organofibrosis, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 1-21.

29. A pharmaceutical composition for use in treating leukemia, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 1-21.

30. A pharmaceutical composition for use in treating articular rheumatism, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically accept-

able salts according to any one of Claims 1-21.

31. A pharmaceutical composition for use in treating glomerulonephritis, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to Claim 5, 8 or 12.

32. A pharmaceutical composition for use in treating tumors, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19.

33. A pharmaceutical composition for use in treating leukemia, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19.

34. A pharmaceutical composition for use in treating articular rheumatism, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19.

35. A method for treating neoplastic tumors, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for neoplastic tumors.

36. A method for treating psoriasis, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for psoriasis.

37. A method for treating atherosclerosis, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for atherosclerosis.

38. A method for treating restenosis after percutaneous coronary angioplasty or bypass surgery, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for restenosis after percutaneous coronary angioplasty or bypass surgery.

39. A method for treating glomerulonephritis, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for glomerulonephritis.

40. A method for treating organofibrosis, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for organofibrosis.

41. A method for treating leukemia, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for leukemia.

42. A method for treating articular rheumatism, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for articular rheumatism.

43. A method for treating glomerulonephritis, which comprises administering an effective amount of the compounds according to Claim 5, 8 or 12 to patients who need treatment for glomerulonephritis.

44. A method for treating tumors, which comprises administering an effective amount of the compounds according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19 to patients who need treatment for tumors.

45. A method for treating leukemia, which comprises administering an effective amount of the compounds according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19 to patients who need treatment for leukemia.

46. A method for treating articular rheumatism, which comprises administering an effective amount of the compounds according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19 to patients who need treatment for articular rheumatism.

47. Use of the compounds according to any one of Claims 1 to 21 for manufacturing pharmaceutical compositions.

48. Use of the compounds according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19 for manufacturing antitumor agents.

49. Use of the compounds according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19 for manufacturing therapeutic agents for articular rheumatism.